CLAIMS

1. A process for producing a pharmaceutical composition comprising the steps:

(a) forming a feed solution comprising a drug, a concentration-enhancing polymer and a solvent;

(b) directing said feed solution to a spray-drying apparatus comprising

(i) a drying chamber having a volume V_{dryer} and a height H,

(ii) atomizing means for atomizing said feed solution into droplets,

(iii) a source of heated drying gas for drying said droplets, said source delivering said drying gas to said drying chamber at a flow rate of G, and

(iv) gas-dispersing means for dispersing said drying gas into said drying chamber, said gas-dispersing means causing organized plug flow of said drying gas,

wherein V_{dryer} is measured in m^3,

H is at least 1 m,

G is measured in m^3/sec,

and wherein the following mathematical relationship is satisfied

$$\frac{V_{dryer}}{G} \geq 10 \text{ seconds};$$

(c) atomizing said feed solution into droplets in said drying chamber by said atomizing means, said droplets having an average diameter of at least 50 μm and a D_{10} of at least 10 μm;

(d) contacting said droplets with said heated drying gas to form particulates of a solid

amorphous dispersion of said drug and said concentration-enhancing polymer; and

(e) collecting said particulates,

wherein said concentration-enhancing polymer is present in said solution in an amount sufficient that said solid amorphous dispersion provides concentration enhancement of said drug in a use environment relative to a control composition consisting essentially of an equivalent amount of said drug alone.

2. The process of claim 1 wherein said gas-dispersing means is a perforated plate.

3. The process of claim 2 wherein said perforated plate has perforations occupying about 1% of its surface area.

4. The process of claim 3 wherein the density of said perforations near the center of said plate is about 25% the density of said perforations in the outer part of said plate.

5. The process of claim 1 wherein said drying gas has an inlet temperature of from about 60° to about 300°C.

6. The process of claim 5 wherein said drying gas has an outlet temperature of from about 0° to about 100°C.

7. The process of claim 1 wherein said droplets have a D_{10} of at least 15 μm.

8. The process of claim 7 wherein said droplets have a D_{10} of at least 20 μm.

9. The process of claim 1 wherein said droplets have a Span of less than about 3.

10. The process of claim 1 wherein said droplets have a Span of less than about 2.

11. The process of claim 1 wherein at least 80 vol% of said particulates have diameters of greater than 10 μm.

12. The process of claim 11 wherein at least 90 vol% of said particulates have diameters of greater than 10 μm.

13. The process of claim 1 wherein said drug in said dispersion is substantially amorphous, and said dispersion is substantially homogeneous.

14. The process of claim 1 wherein said composition provides a maximum drug concentration of said drug in said use environment that is at least about 1.25-fold that provided by said control composition.

15. The process of claim 1 wherein said composition provides in said use environment an area under the drug concentration versus time curve for any 90-minute period from the time of introduction to about 270 minutes following introduction to said use environment that is at least 1.25-fold that provided by said control composition.

16. The process of claim 1 wherein said composition provides a relative bioavailability of said drug that is at least 1.25-fold that of said control composition.

17. The process of claim 1 wherein said drug is selected from the group consisting of antihypertensives, antianxiety agents, anticlotting agents, anticonvulsants, blood glucose-lowering agents, decongestants, antihistamines, antitussives, antineoplastics, beta blockers, anti-inflammatories, antipsychotic agents, cognitive enhancers, anti-atherosclerotic agents, cholesterol-reducing agents,

antiobesity agents, autoimmune disorder agents, anti-impotence agents, antibacterial and antifungal agents, hypnotic agents, anti-Parkinsonism agents, anti-Alzheimer's disease agents, antibiotics, anti-depressants, antiviral agents, glycogen phosphorylase inhibitors, and cholesterol ester transfer protein inhibitors.

18. The process of claim 17 wherein said drug is selected from the group consisting of [R-(R*S*)]-5-chloro-N-[2-hydroxy-3-{methoxymethylamino}-3-oxo-1-(phenylmethyl)propyl-1H-indole-2-carboxamide; 5-chloro-1H-indole-2-carboxylic acid [(1S)-benzyl-(2R)-hydroxy-3-((3R,4S)-dihydroxy-pyrrolidin-1-yl-)-3-oxypropyl]amide; [2R,4S]-4-[acetyl-(3,5-bis-trifluoromethyl-benzyl)-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester; [2R,4S] 4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid ethyl ester; and [2R,4S] 4-[(3,5-bis-trifluoromethyl-benzyl)-methoxycarbonyl-amino]-2-ethyl-6-trifluoromethyl-3,4-dihydro-2H-quinoline-1-carboxylic acid isopropyl ester.

19. The process of claim 1 wherein said concentration-enhancing polymer is selected from the group consisting of ionizable cellulosic polymers, non-ionizable cellulosic polymers, ionizable non-cellulosic polymers, non-ionizable non-cellulosic polymers, neutralized acidic polymers and blends thereof.

20. The process of claim 19 wherein said polymer is selected from the group consisting of hydroxypropyl methyl cellulose, hydroxypropyl cellulose, carboxymethyl ethyl cellulose, hydroxypropyl methyl cellulose acetate succinate, hydroxypropyl methyl cellulose phthalate, cellulose acetate phthalate, cellulose acetate trimellitate, polyvinyl alcohols that have at least a portion of their repeat units in

hydrolyzed form, polyvinyl pyrrolidone, poloxamers and blends thereof.

21. The product of the process of any of claims 1-20.

22. A composition comprising a plurality of solid amorphous dispersion particles comprising a drug and a polymer wherein said particles have an average diameter of at least 40 μm and a bulk specific volume of less than 5 mL/g, and wherein at least 80 vol% of said particles have diameters of greater than 10 μm.

23. The composition of claim 22 wherein at least 90 vol% of said particles have diameters of greater than 10 μm.

24. The composition of claim 22 wherein said particles have an average diameter of at least 50 μm.

25. The composition of claim 22 wherein said particles have a bulk specific volume of less than 4 mL/g.